PRELIMINARY PROGRAM
MONTANA STATE UNIVERSITY/UCLA SYMPOSIUM
ON MOLECULAR AND CELLULAR BIOLOGY

THE MOLECULAR BASIS FOR OXIDATIVE DAMAGE BY LEUKOCYTES
JANUARY 28 - FEBURARY 3, 1991

Organizers:

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The link between disease and the production of toxic oxygen species by inflammatory cells provides exciting opportunities for molecular and cellular biochemistry to alleviate a variety of human afflictions. Recent progress in understanding molecular events in the regulation of superoxide production by leukocytes parallels an expanded growth in understanding of the molecular basis of damage to tissue components by activated oxygen species. Characterization of newly discovered molecular constituents of the superoxide generating system and analysis of their organization in the plasma membrane of the cell provides clues to appropriate and inappropriate activation mechanisms in vivo. Improved methods for monitoring cellular oxidative damage including DNA adducts, modified proteins, lipid peroxides, and cytotoxic aldehydes permit evaluation of specific molecular targets in injured cells. Pathophysiological evidence from such diverse areas as the study of ischemia, atherosclerosis, pulmonary inflammation and other inflammatory diseases clearly point to key roles of toxic oxygen species in the genesis or progression of such conditions. Thus, synergy between biochemistry and pathophysiology delineates paths to prevention, control or therapy. The central goal of The Symposium is to facilitate a synthesis of the molecular views of biochemists, physicians, and leukocyte biologists on the production of activated oxygen species by inflammatory cells, the biochemistry of the tissue products generated, and their roles in disease.

The integration of different research approaches to explain the origin and propagation of inflammatory disease is a significant problem. Usually scientific exchange in the field is confined by topical content to three areas: the production of oxy-radicals by leukocytes, the effects of the progragated activated oxygen species radicals on biochemical and biological systems, and the role of these effects in human disease. Thus quite often, for example, physicians attending meetings concentrating on oxy-radical related disease processes remain unaware of the recent findings and emerging principles from the other two research areas. If we are to arrive at an understanding of the oxygen radical related processes that will have a major impact on the health of humans, then it is essential that a more

integrated approach be used. Consequently, the primary goal of the proposed meeting is to bring together biochemists and physicians, on a daily, session-by-session basis to stimulate discussion, cross-fertilize areas, and thus integrate results of recent research efforts.

The sessions in the planned program consist of presentations by basic and clinical scientists involved in investigations on the production of oxygen radicals by inflammatory cells, the biochemistry of the generated products, and their role in disease. Paralleld workshops on the evening of the arrival day will aim to teach the chemistry of activated oxygen species to biologists and physicians and neutrophil biology to chemists and biochemists. The plenary session on Monday evening will present an overview and define the goals of the meeting.

GENERAL SCHEDULE

Conference Arrival Date	1/27/91-1/28/91
Conference Start Date	1/28/91
Conference Last Session	2/02/91 a.m.
Conference Leave Date	2/03/91

Session Topics Include: Chemistry & Biochemistry of Activated Oxygen; Superoxide: Generation & Targets; Mediators of O_2^- Production; Regulatory Events in O_2^- Production and Damage; Role of Leukocyte & Target Surfaces in the Generation of O_2^-; Tissue Concentration of Activated Oxygen Species and Their Influence on Injury; Pathology of Unregulated O_2^- Production; Strategies for the Control of O_2^- Dependent Pathology. Topics of specific interest in three poster sessions.

MOLECULAR BASIS FOR OXIDATIVE DAMAGE BY LEUKOCYTES
January 28, 1991 - February 2, 1991

Monday, January 28, 1991

All Day: Arrival at Big Sky of Montana Resort

Late Afternoon: Introductory Workshops (Stimultaneous)

Goal: To provide pertinent summaries of a) Oxygen Chemistry for the biologist and physician; b) biology of neutrophils for chemists or biochemists studying toxic oxygen species.

Workshop I. Basic Chemistry of Toxic Oxygen Species
Donald Sawyer, Ph.D., Professor/Department of Chemistry/Texas A & M

Workshop II. Biology of Neutrophils
Robert A. Clark, M.D., Professor/Univ. of Iowa Med. School/319-356-2756

Monday, January 28, Evening

SESSION 1.

Welcome Address: William Tietz, Ph.D., President
Montana State University, 406-994-2341

Orientation: Big Sky of Montana

Introduction: Edwin H. Abbott, Ph.D., Head, Chemistry Department
Montana State University, 406-994-5390

Plenary Address: Review of the central concepts of the chemistry, biology, and biochemistry of superoxide and other activated oxygen species. Statement of problems yet to be solved.
"The Chemistry and Biology of Superoxide"
Irwin Fridovich, PhD/Prof/Biochemistry/Duke Univ. Medical Center/919-684-5122

Tuesday, January 29, 1991, a.m.

SESSION 2. - SUPEROXIDE: GENERATION AND TARGETS

Goals: Description of the molecules of superoxide production and damage.

Chairman: Bernard M. Babior, MD, PhD/Member/Dept. of Basic & Clinical Research/ Scripps Clinic and Research Foundation/619-554-8258

Overview: "History of Progress in the Molecular Analysis of Leukocyte O_2^- Production"
Bernard M. Babior, MD, PhD/Member/Dept. of Basic & Clinical Research/Scripps Clinic and Research Foundation/619-554-8258

"Superoxide Production by Human Phagocytes"
John Curnutte, MD,PhD/Assoc. Member/Biochemistry/Scripps Clinic & Research Foundation/619-554-9784

"Molecular Mechanisms of Microbial Killing"
Seymour Klebanoff,PhD,MD/Prof/Medicine/Univ. of Wash. Medical School/206-543-7902

"Effects of Activated Oxygen Species on Membranes as Detected by Fluorescence and Biochemical Techniques"
Alex Sevanian, PhD/Prof/Toxicology/University of Southern California/213-224-7352

"Molecular Damage in Cells by Oxygen Radicals"
Charles G. Cochrane, MD/Member/Immunology/Scripps Clinic & Research Foundation/619-554-8212

"Oxidant Injury in Sodium Transporting Epithelia"
Bruce Freeman,PhD/Assoc. Prof/Anesth. & Biochemistry/University of Alabama

Tuesday, January 29, 1991, p.m.

SESSION 3. - ELECTRON TRANSPORT AND REDUCTION OF MOLECULAR OXYGEN TO SUPEROXIDE BY CYTOCHROMES

Goals: Evaluation of Human Neutrophil Cytochrome b as the Terminal Component of the Phagocyte Superoxide Generating System

Chairman: Harry Gray, PhD/Prof/Chemistry/Calif. Inst. of Tech./818-356-6502

"The b Cytochrome of Human Phagocytes"
Charles A. Parkos, MD,PhD./Resident/Pathology/Brigham & Williams Hospital/617-732-7536

"Molecular Associations of Neutrophil Cytochrome b"
Mark T. Quinn, PhD/Res. Associate/Chemistry/Montana State University/406-994-4166

"Radical Reactions in Hemeproteins"
Ortiz de Montellano, PhD/Professor/Pharmacology/Univ. of Calif., San Francisco/415-476-2903

"Electron Transferases"
Harry Gray, PhD/Professor/Chemistry/Calif. Institute of Technology/818-356-6502

POSTER SESSION

Wednesday, January 30, 1991, a.m.

SESSION 4. - REGULATORY EVENTS IN $O_2^{\cdot}$ PRODUCTION AND DAMAGE

Goals: Discussion of the relevant events in cells that alter feedback and perturb regulation of $O_2^{\cdot}$ production and damage produced by inappropriate $O_2^{\cdot}$ generation.

Chairman: Filipo Rossi, MD/Prof/Instituto di Patologia Generale/ Univer. degli Studi Verona

"Molecular Mechanism of Activation of Leukocyte Superoxide Production"
Linda McPhail, PhD/Assoc. Prof/Biochemistry/Bowman Gray School of Med./914-748-2621

"Molecular Dissection of the Leukocyte Superoxide Generating System"
Robert A. Clark, MD/Prof/Medicine/University of Iowa Medical School/319-356-2745

"Chemotactic and Pathogenic Activity of 4-hydroxyalkenals Towards Neutrophils"
Hermann Esterbauer, PhD/Prof/Biochemistry/University of Graz, Austria

"Perturbation of Arachidonate Metabolism & Membrane Function by Oxidants"
Henry J. Forman,PhD/Assoc. Prof/Pediatrics & Oncology/Univ. of So. Calif./213-224-4662

"Damage to Phagocytosis Adhesion Receptors by Leukocyte Toxic Oxygen Species"
Hattie D. Gresham, PhD/Asst. Prof/Infectious Diseases/Washington University

"Role of Oxidized LDL in the Formation of Atherosclerotic Lesions"
Daniel Steinberg, MD, PhD/Prof/Dept. of Medicine/UC - San Diego/619-452-4402

Wednesday, January 30, 1991, p.m.

SESSION 5. - ROLE OF LEUKOCYTE AND TARGET SURFACES IN THE GENERATION OF SUPEROXIDE ANION.

Goals: Evaluate the organization of the leukocyte PM and the significance of the contact between leukocyte surfaces and their targets in superoxide production?

Chairman: Stephen Weiss, MD/Assoc. Prof/Internal Med./Univer. Michigan Medical Center/313-763-4723

"Organization of the Leukocyte Plasma Membrane Components of Superoxide Production"
Algirdas Jesaitis,PhD/Professor/Chemistry/Montana State University/406-994-5390

"Potentiation of the Oxidative Burst by Occupancy of Laminin Receptors"
Marilyn C. Pike, PhD/Assoc. Prof/Arithritis Unit/Mass. General Hospital

"Relationship of Leukocyte Adhesion, Superoxide Generation and Injury"
John M. Harlan, MD/Assoc. Prof/Medicine/Univ. of Wash. Med. School/206-223-3157

POSTER SESSION

Thursday, January 31, 1991, All Day

SESSION 6. - WINTER TOUR OF YELLOWSTONE NATIONAL PARK

Goals: Foster closer personal and scientific ties with a winter tour of Yellowstone National Park. Twelve person parties for snow cat and cross country ski travel will be arranged according to a **cross section** of scientific interests.

7.30 am:	Leave Big Sky Convention Center
9.00 am:	Enter Yellowstone National Park, via West Yellowstone entrance. Change from buses into snowcats.
12.00 pm:	Lunch at the Old Faithful Inn
2.00 pm:	Continue tour of Yellowstone Park
5.00 pm:	End of tour in West Yellowstone
7.00 pm:	Arrival at Big Sky Resort
7:30 pm:	Informal Buffet Dinner

POSTER SESSION

Friday, February 1, 1991, a.m.

SESSION 7. - TOWARD DETERMINATION OF TISSUE CONCENTRATIONS OF ACTIVATED OXYGEN SPECIES

Goals: It has been very difficult to be certain of the damaging concentrations of activated oxygen species in tissues. This session will focus attention on the current state of the art in this area.

Chairman: Edward A. Dratz, PhD/Professor/Chemistry/Montana State University/406-994-5378

"The $O_2^{\cdot}$ Forming NADPH Oxidase - Mechanisms of Activation and Function"
Filipo Rossi, MD/Prof/Instituto di Patologia Generale/Univer. degli Studi Verona

"Determining Phagocyte-Produced $O_2^{\cdot}$ Levels in Tissues"
Stephen J. Weiss, MD/Assoc. Prof/Internal Med./Univ. Mich. Med. Ctr./313-763-4723

"Mechanism of the Inactivation of Cellular Glyceraldehyde-3-Phosphate Dehydrogenase by H_2O_2"
Paul A. Hyslop, PhD/Research Scientist/Eli Lilly Research Labs/317-276-7490

"Tissue Sources of Activated Oxygen Species During Oxidant Stress and Ischemia with Reperfusion"
Matthew D. Grisham, PhD/Assoc. Prof/Biochemistry/Univ. of So. Alabama, College of Medicine/205-460-6402

"Determination of Lipid Peroxides and Toxic Breakdown Products of Peroxides in Tissues"
Erik van Kuijk, MD,PhD/Asst. Prof/Medical Biochemistry/Montana State University/406-994-4801

"Determinating the Effects of Oxy-radicals on DNA"
Bruce Ames, PhD/Professor/Biochemistry/Univ. Calif. Berkeley/415-642-5165

Friday, February 1, 1991, p.m.

SESSION 8. - SYMPOSIUM BANQUET

Symposium Overview Address:
"Superoxide Production and Human Disease"
Joe M. McCord, PhD/Prof/Chairman/Biochemistry/Univ. South Alabama/205-460-6402

Saturday, February 2, 1991, a.m.

SESSION 10. - STRATEGIES FOR THE CONTROL OF O_2^- DEPENDENT PATHOLOGY.

Goals: Discussion of Ways to Prevent Tissue Damage.

Chairman: Charles Cochrane, MD/Member/Immunology/Scripps Clinic & Research Foundation/619-554-8212

"Prevention of Oxidant Injury by Neutrophils"
John Repine, MD/Professor/Medicine/Webb Waring Lung Institute/Univ. Of Colorado, Denver 80204

"Inhibition of Activation of Superoxide Generation by Cytochrome b-derived Peptides"
Harry Malech, Bacterial Diseases Section/NIAID/LCI/Bethesda, MD, 20892/301-496-1343

"Biochemistry of Toxic Oxygen Species and Antioxidants"
Edward A. Dratz, PhD/Prof/Chemistry/Montana State University/406-994-5378

"NIH Focus on the Prevention of O_2^- Dependent Tissue Damage"
John Gallin, MD/Director, NIH Intramural Research Program/301-496-3006

"Molecular Intervention in Inflammatory Disease: Academic-Industrial Perspectives"
Ralph Snyderman, Chancellor, Duke University Medical School/Durham, NC, 27710/919-684-2255

Saturday, February 2, 1991, p.m.

SESSION 9. - PATHOLOGY OF UNREGULATED $O_2^{\cdot}$ PRODUCTION

Goals: Discussion of the molecular basis of pathology arising from unregulated $O_2^{\cdot}$ production. How are oxidant species linked to molecular targets?

Chairman: Irwin Fridovich, PhD/Prof/Biochemistry/Duke Univ. Med. Center/919-684-5122

"Amplification and Control of Tissue Injury by Leukocyte Oxidant Production"
Peter Ward, PhD/Professor/Chairman/Pathology/University of Michigan/313-763-6384

"Role of Toxic Oxygen Metabolites in Ischemia"
Myron L. Weisfeldt, MD/Professor/Anesth./J. Hopkins Univ. Sch. of Medicine/301-955-3097

"Prevention of Ischemic Reperfusion Tissue Injury During Surgery"
George C. Bulkley, MD/Prof/Surgery/Johns Hopkins Univ. Sch. of Med./301-955-3097

The Daily Program will include a Poster Session (Tuesday, Wednesday and Thursday) from 4:00 to 5:30 p.m. on topics determined by abstract submission. The posters will remain up for 24 hours in an easily accessible area of the Conference Center.